REMARKS

Upon entry of this amendment, claims 54, 58-65, and 81-82 are pending. Claims 54, 59, 60, and 63 have been amended. New claims 81-82 have been added. Support for the amendment to claim 54 is found *inter alia* original PCT claim 29. Support for the amendment to claim 63 is found *inter alia* pages 63 and 66 of the published PCT application. Support for new claims 81 and 82 is found *inter alia* page 15, lines 3-4 and 22-24. Claims 1-53, 55-57, and 66-80 have been canceled. Applicants reserve the right to prosecute the cancelled subject matter, as well as the originally presented claims in continuing applications.

No new matter is added.

I. § 112 Rejection, first paragraph

A. Claims 75-79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Claims 75-79 have been canceled. As such, Applicants submit that the rejection is moot and request withdrawal.

B. Claims 54-65 and 75-79 are rejected under 35 U.S.C. 112, first paragraph, because the Office Action states that the specification does not reasonably provide enablement for the claimed mechanisms and the diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Office Action states that claims 54-65 and 75-79 are drawn to all nervous system diseases known and to those that may be found in the future because claims 75-79 are drawn to mechanism by which the instant compounds work in the body. And further, the Office Action goes on to say that there is no evidence the instant compounds would treat such diseases.

Applicants respectfully disagree. However, in the interest of expediting prosecution, Applicants have amended claim 54 to recite Alzheimer's disease and have also significantly amendment the breadth of the compounds recited in claim 54 to a single

formula. Applicants note that all of the remaining claims 58-65 and 81-82 properly depend from claim 54. Claims 55-57 and 66-79 have been canceled and as such, the rejection is moot with respect to those claims. Applicants acknowledge the Examiner's statement that by limiting the disease to Alzheimer's the rejection would be overcome (See, the first full paragraph on page 7 of the Office Action). In view of the amended claims and the Examiner's statement, Applicants request that the rejection be withdrawn.

II. § 112 Rejection, second paragraph

A. Claims 54-65 and 75-79 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that the rejection is for the reasons discussed with reference to the 112, first paragraph rejection and refers to the suggestion to amend the claims to Alzheimer's. In view of the amended claims, Applicants assert that the subject matter is not indefinite and request withdrawal of the rejection.

B. Claims 54-65 and 75-79 are rendered indefinite because they use the term "combination" which the Examiner says in every occurrence is subject to more than one interpretation and therefore renders claims 54-65 and 75-80 indefinite. Claim 54 has been amended to delete the term "combination". All of the remaining claims 58-65 and 81-82 properly depend from claim 54 and none recite the term "combination". Further, claims 55-57 and 66-79 have been canceled and as such, the rejection is moot with respect to those claims. In view of the amended claims, Applicants request withdrawal of the rejection.

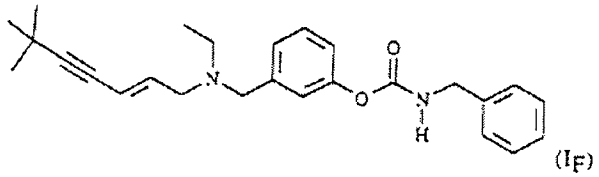
II. 35 USC § 102

Eight documents were cited against the invention, alleging that it lacks novelty in view of the cited documents. For all eight documents, claims 54-65 and 75-80 were rejected under 35 U.S.C. 102(b). Claims 55-57 and 75-80 have been canceled. Thus, the rejection is moot with respect to these claims.

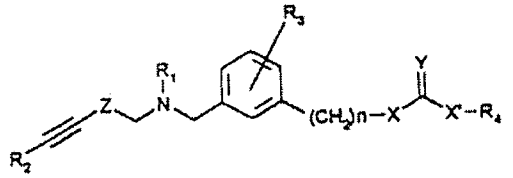
Applicants submit that the claimed invention as-amended is novel over the documents cited by the Examiner. Each of the eight documents cited in the Office Action is discussed below regarding novelty in view of the amended claims.

1. Jean-Pierre et al. FR 2719047 (referred to as "FR '047") discloses compounds that inhibit squalene epoxidase and acetylCoA-cholesterol-O-acyl transferase (ACAT)/antioxidants (See, FR '047 at p. 3, lines 4-17; p. 22, line 25 - p. 24, line 23). Nowhere does FR '047 state that its compounds are useful in the field of cholinesterase inhibition. The Office Action cites the examples on pp. 17-25 e.g., example F (compound IF) at page 22, pp. 1-3 which discloses formula I, and the claims.

The chemical structures for compound IF and formula I are shown below:

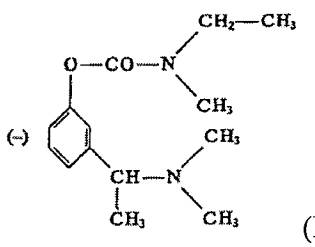


(I_F)

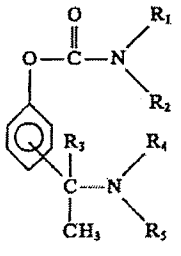


(I). The FR '047 compounds do not overlap with the formula covering the claimed compounds because the tertiary nitrogen of the FR '047 compounds is substituted with $-CH_2-Z-\equiv-R_2$ e.g., See compound IF: $-CH_2-CH{=}CH-\equiv-C(CH_3)_3$. This substitution on the nitrogen corresponds with the values R_4 or R_5 in the formula of the instant claims. Applicants submit that R_4 and R_5 do not cover the acetylene moiety as found in the examples on pp. 17-25, compound IF or formula I. As-amended, the formula covering the claimed compounds does not overlap with the formula of FR '047. The FR '047 compounds do not fall under the claimed formula as-amended. Thus, the claimed invention is novel over FR '047.

2. Sandoz-Patent-gambH, DE 3805744 (referred to as "DE '744") relates to compounds having the Formula I and I':



(I)(p.2-3) and

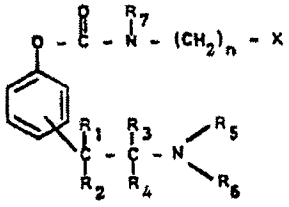


(I')(p.2). The Office Action states that the prior art is applied as set forth in the Int. Search Report of PCT/US04/034548 and examples on pp. 2-3.

In Formula I of DE '744, the carbamate nitrogen atom is substituted with two alkyl groups, an ethyl group and a methyl group. Because the formula covering the claimed compounds does not allow for R_1 and R_2 to both be unsubstituted alkyl, the claimed invention is novel over Formula I.

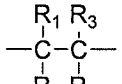
In Formula I' of DE '744, the carbamate nitrogen is substituted with R_1 and R_2. The values for R_1 and R_2 are as follows: R_1 is hydrogen, lower alkyl, cyclohexyl, allyl or benzyl and R_2 is hydrogen, methyl, ethyl or propyl. As-amended, the formula covering the claimed compounds does not overlap with Formula I'. Specifically, there is no overlap because the formula covering the claimed compounds does not allow for R_2 to be hydrogen or unsubstituted alkyl. And also, an "aralkylgroup" in the claimed invention is defined as being an aryl group connected to a straight-chain or branched alkyl having from three to five carbon atoms, thus there is no overlap with the claimed R_2 and the value R_1 is benzyl in DE '744, which has only one carbon atom. The DE '744 compounds do not fall under the claimed formula as-amended. Thus, the claimed invention is novel over DE '744.

3. Terni et al. WO 96/02524 (referred to herein as "Terni") relates to compounds for use as anticholinesterase substances having the Formula (I):



(I). The Office Action states that Terni discloses similar compounds and their method of use for treating nervous system diseases. Applicants respectfully disagree.

Formula I of Terni **requires** that the left-hand portion of the compounds contain two carbon atoms between the central phenyl ring and the terminal $-NR_5R_6$ group

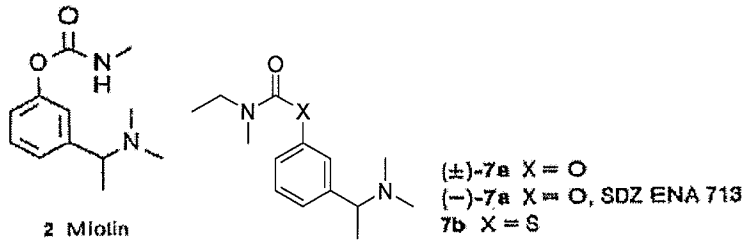


). Because the claimed compounds only require a single carbon atom between the central phenyl ring and the terminal $-NR_4R_5$ group, the claimed invention is novel over Terni. The Terni compounds do not fall under the claimed formula as-amended. Thus, the claimed invention is novel over Terni.

4. Amstutz et al. Helvetica Chimica Acta (1990), vol. 73, pp. 739-753 (referred to as "Amstutz") relates to compounds for acetylcholinesterase inhibition. The Office Action states that Amstutz discloses similar compounds and their method of use for treating nervous system diseases and specifically cites the Abstract and compounds 2 and 7 as being relevant. Applicants respectfully disagree.

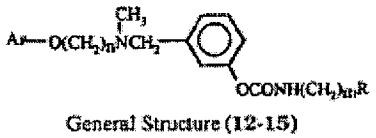
The Abstract of Amstutz describes six-, seven-, and eight-membered **cyclic** phenyl carbamates and refers to their synthesis and potency. The present claims do not cover cyclic phenyl carbamates like those described in the Abstract of Amstutz. As such, the claims are novel over the cyclic compounds described in the Abstract of Amstutz.

The chemical structures of compounds 2 and 7 are shown below:



. Compounds 2 and 7 contain the carbamate groups -OC(O)NHMe and -OC(O)NEtMe respectively. Because the formula covering the claimed compounds does not allow for (1) both R_1 and R_2 to be unsubstituted alkyl and (2) one of R_1 or R_2 to be unsubstituted alkyl and the other to be hydrogen, the compounds 2 and 7 do not fall under the claimed formula as-amended. Thus, the claimed invention is novel over Amstutz.

5. Rampa et al. J. Am. Chem. (2001), vol. 44, pp 3810-3820 (referred to as "Rampa") relates to derivatives of Xanthostigmine for acetylcholinesterase. The Office Action states that Rampa discloses similar compounds and their method of use for treating nervous system diseases and cites the introduction, Charts 1-2, pp. 3810 and compounds 13-14 having the formula:



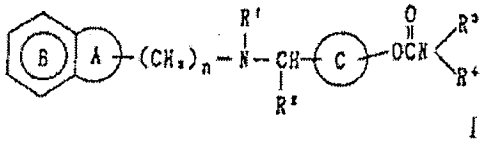
General Structure (12-15)

. Applicants respectfully disagree.

The Rampa compounds do not overlap with the formula covering the claimed compounds because the Rampa compounds contain a carbamate group - $OC(O)NH(CH_2)_mR$, wherein R is CH_3 and m is 0 i.e., $-OC(O)NHCH_3$. Because the formula covering the claimed compounds does not allow for one of R_1 or R_2 to be

unsubstituted alkyl and the other to be hydrogen, the Rampa compounds do not fall under the claimed formula as-amended. Further, the left-hand portion of the molecule contains an aryloxy group which is not covered by the claimed formula. Thus, the claimed invention is novel over Rampa.

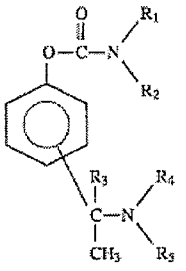
6. Goto et al. JP 3002155 (referred to as "Goto") relates to compounds that are cholinesterase inhibitors for improvement in cerebral function. Goto contains compounds of formula I:



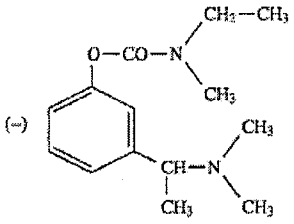
I

The Goto compounds contain the carbamate group -OC(O)NR_3R_4 and R_3 and R_4 are selected from hydrogen and lower alkyl. Because the formula covering the claimed compounds does not allow for (1) R_1 and R_2 to both be unsubstituted alkyl or (2) one of R_1 or R_2 to be unsubstituted alkyl and the other to be hydrogen, the Goto compounds do not fall under the claimed formula as-amended. Further, the Goto compounds require a bicyclic ring wherein ring A is a 5 to 8-membered ring which may contain a heteroatom and ring B is (substituted) benzene ring. Thus, the claimed invention is novel over Goto.

7. Enz, US 5,602,176 (referred to herein as "Enz") relates to compounds that are acetylcholinesterase inhibitors of formula I' and I:



(I') and

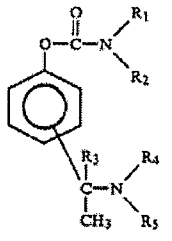


I

(I). For formula I': R_1 is hydrogen, lower alkyl, cyclohexyl, allyl or benzyl, and R_2 is hydrogen, methyl, ethyl or propyl. The Office Action alleges that Enz discloses similar compounds and their method of use for treating nervous system diseases. See compounds I and I'. Applicants respectfully disagree.

Because the formula covering the claimed compounds does not allow for R_1 and R_2 to both be unsubstituted alkyl, the compound of formula I in Enz is not covered by the claimed formula. Further, the claimed formula requires that R_2 is an aralkylgroup. An "aralkylgroup" in the claimed invention is defined as being an aryl group connected to a straight-chain or branched alkyl having from three to five carbon atoms, thus there is no overlap with the value R_1 is benzyl in Enz, which has only one carbon atom. The Enz compounds do not fall under the claimed formula as-amended. Thus, the claimed invention is novel over Enz.

8. Rosin et al., US 4,948,807 (referred to herein as "Rosin") relates to compounds with anticholinesterase activity having the Formula I:



(I). The Office Action alleges that Rosin et al. discloses similar compounds and their method of use for treating nervous system diseases and cites compounds 1-2. Applicants respectfully disagree.

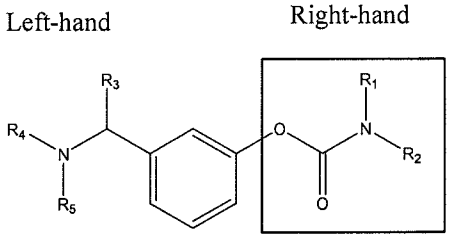
As-amended, the formula covering the claimed compounds does not overlap with Formula I. In Formula I of Rosin, the carbamate nitrogen is R_1 and R_2 where R_1 is hydrogen, lower alkyl, cyclohexyl or benzyl, and R_2 is hydrogen, methyl, ethyl, or propyl. Specifically, there is no overlap because the claimed formula does not allow for R_2 to be hydrogen or unsubstituted alkyl. And, an "aralkylgroup" is defined as being a branched alkyl and having from three to five carbon atoms, thus there is no overlap with the claimed R_2 and the value R_1 is benzyl in Rosin, which has only one carbon atom. The Rosin compounds do not fall under the claimed formula as-amended. Thus, the claimed invention is novel over Rosin.

In view of the arguments presented above, Applicants request withdrawal of the rejection.

II. 35 USC § 103

Claims 54-65 and 75-80 are rejected under 35 U.S.C. 103(a) as being unpatenable over the prior arts listed above (See, page 10 of the Office Action). Claims 55-57 and 75-80 have been canceled. Thus, the rejection is moot with respect to these claims. The Examiner states that the prior art discloses similar compounds, their composition and method of use for treating nervous system diseases. Specifically, the Examiner states that the difference between the instant invention and that of the prior art is that the alkyl chain in the compounds of the Applicants is longer than in the prior art. The Examiner states that in other words, the Applicants have replaced H with alkyl in the compounds of the prior art. The Examiner alleges that one of ordinary skill in the art would have known to replace H with alkyl. Applicants respectfully disagree.

The Examiner asserts that the difference between the compounds of the instant invention and those of the prior art is that the instant compounds are **longer**. Applicants believe that the Examiner's reference to the compounds being "longer" and replacement of a H with alkyl is referring to the right-hand portion of the molecules i.e., the carbamate moiety:



carbamate moiety

Applicants also note that the Examiner refers to the compounds as being adjacent homologs and states that adjacent homologs are prime facie obvious (See, Office Action at page 10).

Applicants submit that these general statements simply do not apply to all of the compounds contained in all eight of the cited documents. First, many of the prior art compounds differ from the claimed compounds at the left-hand portion of the molecule. For example, in at least four of the cited documents (FR '047, Rampa, Goto, and Terni), the left-hand portion of the compounds is **structurally different** from the instant compounds. Specifically, in the left-hand portion of the molecules, the compounds of FR '047 contain an acetylene moiety, the Rampa compounds contain an -Oaryl moiety, the

Terni compounds contain an additional methylene and the compounds of Goto are required to have a bicyclic fused ring.

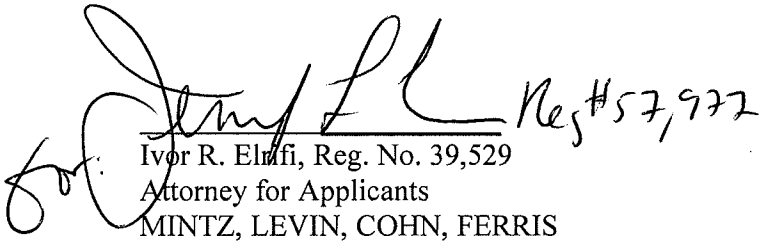
Further, Applicants submit that the claimed compounds and prior art compounds in the remaining 4 references: DE '744, Amstutz, Enz, and Rosin are not adjacent homologs. Section 2144.09 of the MPEP describes "homologs" as compounds differing regularly by the successive addition of the same chemical group *e.g.*, by -CH_2- groups. Applicants submit that the claimed compounds and the prior art compounds differ by **more than** a methylene group on the right-hand side of the molecule. For example, the relevant compounds disclosed in Amstutz have a carbamate nitrogen atom substituted with small alkyl groups and/or hydrogen atoms and **completely lack** the aryl group of the claimed compounds. Similarly, the compounds explicitly disclosed in DE '744, Enz, and Rosin have carbamate nitrogen atoms substituted with small alkyl groups and/or hydrogen atoms and again **completely lack** the aryl group of the claimed compounds. Applicants note that DE '744, Enz, and Rosin each disclose a generic formula wherein one of the groups on the nitrogen carbamate can be benzyl (CH_2-Ph). However, Applicants submit that the difference is **more than** a simple methylene group between these benzyl substituted formulae in the prior art and the claimed compounds containing an aralkylgroup with a branched alkyl group having from 3-5 carbon atoms. As such, these compounds are not adjacent homologs. Further, there is no teaching or suggestion in DE '744, Enz and Rosin to replace one of the hydrogen atoms on the methylene of the benzyl group with a methyl group and then extend the alkyl chain by at least one additional carbon. Specifically, there is no teaching to introduce any more sterically hindered group. It is well known by the skilled medicinal chemist that branched alkyl groups are more sterically hindered than a simple straight chain methylene group. As such, the skilled artisan would not have been able to predict such a replacement would lead to successful compounds.

In view of the arguments presented above, Applicants submit that the claimed invention is not obvious in view of the cited art and request withdrawal of the rejection.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Date: March 25, 2010



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